

REMARKS

This is a full and timely response to the outstanding nonfinal Office Action mailed July 10, 2003. Reconsideration and allowance of the application and presently pending claims, as amended, are respectfully requested.

Present Status of Patent Application

Upon entry of the amendments in this response, claims 8 and 10-16 remain pending in the present application. More specifically, claims 8, 10, and 12-14 are directly amended; claim 9 is canceled without prejudice, waiver, or disclaimer. These amendments and additions are specifically described hereinafter. It is believed that the foregoing amendments and additions add no new matter to the present application.

Indication of Allowable Subject Matter

Applicant greatly appreciates the Examiner's statement in the previous Office Action in which the pending claims have been indicated as allowable. In particular, the Examiner notes that "[f]iling of a certified translation of the priority document would overcome the obviousness art rejection against methods using the *C. utilis* bioB gene." Applicant addresses this request in the Response to Rejections Under 103(a) below.

Compliance with the Sequence Rules

The Examiner requested "confirmation that the sequence filing in the listing in Paper No. 8 is identical to the sequence found in the originally filed specification on pages 10-11." *Office Action* at 4. Applicant hereby confirms that the sequence filing in the listing in Paper No. 8 is identical to the sequence found in the originally filed specification on pages 10-11.

The Examiner also noted that on each of pages 9 and 10 two DNA primers are disclosed without the benefit of SEQ ID NOs. The sequence listing as filed as been amended and, per the requirements of 37 CFR §§ 1.821 - 1.825, the Applicant has provided: (1) a substitute copy of the sequence listing, both in computer readable format and paper copy; (2) a statement that the content of the paper and CRF copies are the same and include

no new matter, and (3) an amendment to the specification to identify the sequences appropriately by SEQ ID NO.

The computer readable diskette contains new SEQ ID NOs. 2-5. The diskettes and the accompanying paper copy were formatted and printed using the PTO's Patent In Version 3.2 software. Applicants believe in good faith that the added sequence listings comply with the Office guidelines.

Statement Under 37 CFR § 1.821(f)

The undersigned asserts that the diskette and paper copy of the amended sequence listing are identical to each other. Further, neither one, nor both combined, add any new matter to the application as originally submitted.

Cancellation of Claim 9

Claim 9 is canceled without prejudice, waiver, or disclaimer. Applicant takes this action merely to reduce the number of disputed issues and to facilitate early allowance and issuance of other claims in the present application. Applicant reserves the right to pursue the subject matter of the canceled claim in a continuing application, if Applicant so chooses, and does not intend to dedicate any of the canceled subject matter to the public.

Response To Objections/Rejections

Response To Objections To Specification

The Office Action states: "The specification was objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. §606.01). The Examiner suggests the following new title:

--Methods for Preparing Yeast with High Biotin Productivity Using Integrated Plasmids Encoding Biotin Synthase--."

Office Action at 5. The title has been replaced with a new title as per the Examiner's suggestion.

The Office Action states: “The specification is objected to for... inconsistencies and/or confusing subject matter.” *Office Action* at 6.

The Applicant responds to each rejection below:

- a. In the specification, the “[biotindase]” has been replaced with “biotindase” on page 3, line 11.
- b. The SEQ ID NO: 1 has been directed to be *C. utilis* sequence on page 7, line 17.
- c. Page 12, lines 13-14 of the specification, notes that “regardless of protein with incomplete 204 amino acids or complete 233 amino acids.” The reason that the *C. utilis* BIO2 gene obtained from Example 2 encodes two kinds of proteins is that the *C. utilis* BIO2 gene has two transcription initiation sites. The protein with 233 amino acids is a complete protein and the protein with 204 amino acids is an incomplete protein; however, the incomplete protein (with 204 amino acids) has the same enzymatic activity as the complete protein (with 233 amino acids).
- d. The “8.2 ng/ml” of biotin produced in wild-type has been replaced with “31.2 ng/ml” on page 14, line 25.
- e. In Table I, the YPD value of WT “8.2” has been replaced with “31.2” which was a typographic error; and the OD_{660nm} value “838” has been deleted since the value was not detected.
- f. As for the ng/ml of m9-101 in YPD (CHY), the value “63” is correct.

Applicant submits that the above amendments are merely for correction of typographical errors, and that no new matter has been introduced. Applicant respectfully requests that the above objections be withdrawn.

Response To Objection To Abstract

The Office Action states:

In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. §608.01(b)).... The Examiner suggests the inclusion of the invention of the *Candida utilis* biotin synthase gene, bioB, as well as its integration into the *C. utilis* genome. Other embodiments include *Saccharomyces cerevisiae* integrating plasmids. Species embodiments are crucial in understanding the specifics of what the disclosure has to offer. Correction is required.

Office Action at 5. The Applicant has amended the Abstract as requested and submits a new Abstract herewith. Applicant therefore respectfully requests that the objection be withdrawn.

Response To Objections To Claims

The Office Action states: "Claims 8-14 are objected to for depending on a non-elected claim, Claim 1. All the limitations of Claim 1 must be amended into Claim 8. Correction is required." *Office Action* at 6. Applicant has made the correction and respectfully requests that the objection be withdrawn.

Response To Claim Rejections Under 35 U.S.C. Section 112, Second Paragraph

Claims 8-14 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." *Office Action* at 6. Applicant respectfully traverses each of the rejections. Nevertheless, to advance prosecution of the patent application, Applicant has complied with the Examiner's suggested corrections regarding the following rejections. Claim 9 has been canceled without prejudice, waiver, or disclaimer, and thus the rejection of that claim has been rendered moot. Applicant has amended claims 8 and 10-14 to place claims 8-14 in condition for allowance.

In the Office Action, the following rejections were made:

“The term ‘high’ is a relative term, which renders the claim indefinite.” *Office Action* at 6. The term “high” in claims 8 and 14 has been replaced with “improved”.

“The term ‘integrated’ in Claim 8, and as the claims depend from Claim 1, is confusing as to whether the term is used as an adjective merely describing the plasmid or as a verb describing what the plasmid is required to do in the method.” *Office Action* at 6. The term “integrated” in claim 8 has been replaced with “integrating”.

“The term ‘assistant DNA sequence for the integration of said plasmid into a host genome’ is unclear, the Examiner cannot find the term ‘assistant DNA’ as a term of art of defined in the specification.” *Office Action* at 6. The term “an assistant DNA sequence for integration of said plasmid into a host genome” in claim 8 has been replaced with ‘an assistant DNA sequence to promote integration into a host genome.’

“The phrase ‘derived from’ [in claims 9-10] is unclear as to its metes and bounds. In today's recombinant technology, numerous mutations to a native *S. cerevisiae* or *C. utilis* sequence can be performed wherein the resulting sequence is still ‘derived from’ *S. cerevisiae* or *C. utilis*. Is the intended limitation --native to-- to indicate a naturally occurring sequence?” *Office Action* at 8. Claim 9 has been canceled without prejudice, waiver, or disclaimer, and thus the rejection of that claim has been rendered moot.

“The antecedent basis of ‘gene of *Candida utilis*’ [in claim 10] is unclear based on the above rejection concerning the term ‘derived from.’” *Office Action* at 8. Claim 10 has been amended to overcome the antecedent basis rejection.

“The term ‘NsiI-BamHI 18s rDNA’ [in claim 11] is unclear as to its exact make-up. The rDNA of yeast are distinct from each other and are large repeating units of DNA.”

Office Action at 8. The “NsiI-BamHI 18s rDNA,” fragment and URA3, as well as HIS3DNA, all belong to *C. utilis* gene fragments.

“The term ‘cycloheximide-resistant gene’ [in claim 12] is unclear.” *Office Action* at 8. The term “cycloheximide-resistant gene” in claim 12 has been replaced with “cycloheximide-resistance gene”.

“The promoters ‘pL41’ and ‘pADH1’ [in claim 13] are unclear as to their exact nature based on the abbreviations used herein. The L41 gene of *C. utilis* and the ADH1 gene of *S. cerevisiae* are clear in the art; moreover, the promoters of these genes are also well defined. However, the ‘p’ abbreviation renders the claims unclear since, in the art, a preceding ‘p’ indicated a plasmid name.” *Office Action* at 9. The “pL41” and “pADH1” promoters in claim 13 have been amended to delete “p”.

“It is unclear exactly how the phrase ‘useful as feed additives, food additives, or cosmetics’ [in claim 14] limits the subject matter of the parent claim.” *Office Action* at 9. The phrase “useful as feed additives, food additives, or cosmetics” in claim 14 has been amended to be “useful in feed additives, food additives, or cosmetics.”

Applicant wishes to clarify that the foregoing amendments are cosmetic in nature and are not made as a condition for obtaining a patent. Applicant further submits that these amendments are non-narrowing and, pursuant to *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 122 S. Ct. 1831 (2002), no prosecution history estoppel arises from these amendments.

Response To Claim Rejections Under 35 U.S.C. Section 102

Claims 8-10 and 14 have been rejected under 35 U.S.C. Section 102(b) as allegedly anticipated by Pearson *et al.* (GB 2216530A) as evidenced by Stearns *et al.* (see PTO-892). Applicant respectfully traverses.

A proper rejection of a claim under 35 U.S.C. §102 requires that a single prior art reference disclose each element of the claim. *See, e.g., W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303, 313 (Fed. Cir. 1983). Anticipation requires that each and every element of the claimed invention be disclosed in a single prior art reference. *See e.g., In re Paulsen*, 30 F.3d 1475, 31 USPQ 2d 1671 (Fed. Cir. 1994); *In re Spada*, 911 F.2d 705, 15 USPQ 2d 1655 (Fed. Cir. 1990). Here, the Examiner has relied on two separate references in order to reject claims 8-10 and 14. Thus, for at least this reason, Applicant requests that the rejection be withdrawn.

Additionally, the Examiner noted “that Claim 11 is omitted from the instant rejection because the HIS3 and URA3 sequences taught by *Stearns et al.* are not from *C. utilis*, nor are they inherent features of all integrating protocols.” *Office Action* at 10. Independent claim 8 has been amended to recite the feature of “an integrating plasmid comprising: (i) a promoter sequence that is functional in yeast, and which is operably linked to a polynucleotide sequence encoding *Candida utilis* biotin synthase.” Applicant submits that at least because the cited references do not teach or suggest this feature, the rejection should be withdrawn.

If independent claim 8 is allowable over the prior art of record, then its dependent claims 9-10 and 14 are allowable as a matter of law, because these dependent claims contain all features/elements/steps of their respective independent claim 8. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988). Additionally and notwithstanding the foregoing reasons for the allowability of claim 8, these dependent claims recite further features/steps and/or combinations of features/steps (as is apparent by examination of the claims themselves) that are patentably distinct from the prior art of record. Hence, there are other reasons why these dependent claims are allowable. Thus, for at least this reason also, Applicant requests that the rejection of the dependent claims be withdrawn.

Response To Claim Rejections Under 35 U.S.C. Section 103

Claims 8-10 and 14 have been rejected under 35 U.S.C. §103(a) as purportedly being obvious over Pearson *et al.* in view of Stearns *et al.* and Hong *et al.* (GenBank Accession Number AF212161). Claims 8-10 and 14 have been rejected under 35 U.S.C. § 103 as purportedly being obvious over Pearson *et al.* in view of Stearns *et al.* and Zhang *et al.* (*Arch Biochem Biophys* (1994) 309(1): 29-35). Claim 11 has been rejected under 35 U.S.C. § 103 as purportedly being obvious over Pearson *et al.* in view of Stearns *et al.* and Rodriguez *et al.* (*FEMS Microbiol Lett* (1998) 165(2): 335-340). Claim 12 has been rejected under 35 U.S.C. § 103 as purportedly being obvious over Pearson *et al.* in view of Stearns *et al.* and Kondo *et al.* (See IDS). Applicant respectfully traverses each of the rejections based on each cited combination of references. The cited combinations fail to establish a *prima facie* case of obviousness.

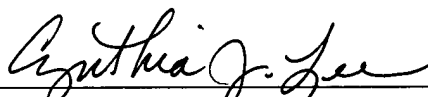
Independent claim 8 has been amended to recite the feature of “an integrating plasmid comprising: (i) a promoter sequence that is functional in yeast, and which is operably linked to a polynucleotide sequence encoding *Candida utilis* biotin synthase.” The Examiner notes “that the *C. utilis* art is intervening art prior to the application’s filing date but after the foreign priority date.” *Office Action* at page 17. For at least the reason that the other cited art does not teach or suggest this feature, the rejection should be withdrawn.

The Examiner has suggested that “[f]iling of a certified translation of the priority document would overcome the obviousness art rejection against methods using the *C. utilis* bioB gene.” *Id.* Applicant submits herewith a translated copy of the priority document, along with a declaration by the translator. For at least this reason as well, Applicant respectfully requests that the rejection be withdrawn.

CONCLUSION

In light of the foregoing amendments and for at least the reasons set forth above, Applicant respectfully submits that all objections and/or rejections have been traversed, rendered moot, and/or accommodated, and that the now pending claims 8 and 10-14 are in condition for allowance. Favorable reconsideration and allowance of the present application and all pending claims are hereby courteously requested. If, in the opinion of the Examiner, a telephone conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (770) 933-9500.

Respectfully submitted,



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Signature - Gloria Simmons